collected at specific time intervals post-administration is analyzed by HPLC or capillary gel electrophoresis (CGE) to determine the amount of oligonucleotide remaining intact in circulation and the nature the of the degradation products.

[0126] Heterocyclic bases amenable to the present invention include both naturally and non-naturally occurring nucleobases and heterocycles. A representative list includes adenine, guanine, cytosine, uridine, and thymine, as well as other synthetic and natural nucleobases such as xanthine, hypoxanthine, 2-aminoadenine, 6-methyl and other alkyl derivatives of adenine and guanine, 2-propyl and other alkyl derivatives of adenine and guanine, 5-halo uracil and cytosine, 6-azo uracil, cytosine and thymine, 5-uracil (pseudo uracil), 4-thiouracil, 8-halo, oxa, amino, thiol, thioalkyl, hydroxyl and other 8-substituted adenines and guanines, 5-trifluoromethyl and other 5-substituted uracils and cytosines, 7-methylguanine. Further heterocyclic bases include those disclosed in United States Patent No. 3,687,808, those disclosed in the *Concise Encyclopedia Of Polymer Science And Engineering*, pages 858-859, Kroschwitz, J.I., ed. John Wiley & Sons, 1990, and those disclosed by Englisch, *et al.*, *Angewandte Chemie, International Edition* 1991, *30*, 613.

[0127] Additional objects, advantages, and novel features of this invention will become apparent to those skilled in the art upon examination of the following examples, which are not intended to be limiting. All oligonucleotide sequences are listed in a standard 5' to 3' order from left to right.

EXAMPLE 1

5'-*O*-DMT-2'-*O*-(2-methoxyethyl)-5-methyl uridine and 5'-*O*-DMT-3'-*O*-(2-methoxyethyl)5-

methyl uridine

[0128] 2',3'-*O*-dibutylstannylene 5-methyl uridine (345 g) (prepared as per: Wagner *et al.*, *J. Org. Chem.*, 1974, *39*, 24) was alkylated with 2-methoxyethyl bromide (196 g) in the presence of tetrabutylammonium iodide (235 g) in DMF (3 L) at 70 °C to give a mixture of 2'-*O*- and 3'-*O*-(2-methoxyethyl)-5-methyl uridine (150 g) in nearly 1:1 ratio of isomers. The mixture was treated with DMT chloride (110 g, DMT-Cl) in pyridine (1 L) to give a mixture of the 5'-*O*-DMT-nucleosides. After the standard work-up the isomers were separated by silica gel column chromatography. The 2'-isomer eluted first, followed by the 3'-isomer.

EXAMPLE 2

5'-*O*-DMT-3'-*O*-(2-methoxyethyl)-5-methyl-uridine-2'-*O*-(2-cyanoethyl-N,N-diisopropyl) phosphoramidite

[0129] 5'-*O*-DMT-3'-*O*-(2-methoxyethyl)-5-methyluridine (5 g, .008 mol) was dissolved in CH_2Cl_2 (30 mL) and to this solution, under argon, diisopropylaminotetrazolide (0.415 g) and 2-cyanoethoxy-N,N-diisopropyl phosphoramidite (3.9 mL) were added. The reaction was stirred overnight. The solvent was evaporated and the residue was applied to silica column and eluted with ethyl acetate to give 3.75 g title compound.

EXAMPLE 3

5'-*O*-DMT-3'-*O*-(2-methoxyethyl)-N^4-benzoyl-5-methyl-cytidine

[0130] 5'-*O*-DMT-3'-*O*-(2-methoxyethyl)-5-methyl uridine (15 g) was treated with 150 mL

anhydrous pyridine and 4.5 mL of acetic anhydride under argon and stirred overnight. Pyridine was evaporated and the residue was partitioned between 200 mL of saturated $NaHCO_3$ solution and 200 mL of ethylacetate. The organic layer was dried (anhydrous $MgSO_4$) and evaporated to give 16 g of 2'-acetoxy-5'-*O*-(DMT)-3'-*O*-(2-methoxyethyl)-5-methyl uridine.

[0131] To an ice-cold solution of triazole (19.9 g) in triethylamine (50 mL) and acetonitrile (150 mL), with mechanical stirring, 9 mL of $POCl_3$ was added dropwise. After the addition, the ice bath was removed and the mixture stirred for 30 min. The 2'-acetoxy-5'-*O*-(DMT)-3'-*O*-(2-methoxyethyl)-5-methyl uridine (16 g in 50 mL CH_3CN) was added dropwise to the above solution with the receiving flask kept at ice bath temperatures. After 2 hrs, TLC indicated a faster moving nucleoside, C-4-triazole-derivative. The reaction flask was evaporated and the nucleoside was partitioned between ethylacetate (500 mL) and $NaHCO_3$ (500 mL). The organic layer was washed with saturated NaCl solution, dried (anhydrous $NgSO_4$) and evaporated to give 15 g of C-4-triazole nucleoside. This compound was then dissolved in 2:1 mixture of NH_4OH/dioxane (100 mL:200 mL) and stirred overnight. TLC indicated disappearance of the starting material. The solution was evaporated and dissolved in methanol to crystallize out 9.6 g of 5'-*O*-(DMT)-3'-*O*-(2-methoxyethyl)5-methyl cytidine.

[0132] 5'-*O*-DMT-3'-*O*-(2-methoxyethyl)-5-methyl cytidine (9.6 g, 0.015 mol) was dissolved in 50 mL of DMF and treated with 7.37 g of benzoic anhydride. After 24 hrs of stirring, DMF was evaporated and the residue was loaded on silica column and eluted with 1:1 hexane:ethylacetate to give the desired nucleoside.